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Review Article

MEDICINAL PLANTS OF RAJASTHAN (INDIA) WITH ANTIDIABETIC POTENTIAL

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ABSTRACT
Rajasthan has a rich heritage of traditional system of medicine and many medicinally useful plants are found growing wildly because of vast area and variety of agro-climatic conditions. These plants are being used for the treatment of many human ailments including diabetes. Plants that are specifically employed for the treatment of diabetes are *Acacia nilotica, Acacia senegal, Aegle marmelos, Calotropis procera, Capparis deciduas, Cassia auriculata, Cassia sophera, Cayratia trifolia, Cyamopsis tetragonoloba, Dalbergia sisso, Gymnema sylvestre, Momordica charantia, Syzygium cumini, Withania somnifera.* This article aims to provide a comprehensive review on the some plants of Rajasthan having antidiabetic potential.
KEYWORDS: Diabetes mellitus, antidiabetic, ethnomedicine

INTRODUCTION

Diabetes mellitus is one of the most common chronic diseases in nearly all countries[1]. This disease is characterized by hyperglycemia resulting from reduced (or absent) secretion of insulin, often coupled with reduced sensitivity to its action (insulin resistance)[2].

Diabetes mellitus fall into three broad categories: Type 1, Type 2, and Gestational diabetes. Type 1 diabetes mellitus is characterized by loss of insulin producing β-cells of the islets of Langerhans in the pancreas leading to insulin deficiency. This type of diabetes can affect children or adults and is traditionally termed "juvenile diabetes" as it represents a majority of the diabetes cases in children[3]. This type is less common and has lower degree of genetic predisposition. Type 2 diabetes mellitus is the most common type and characterized by insulin resistance which may be combined with relatively reduced insulin secretion. This type has higher degree of genetic predisposition and generally has a late onset (past middle age). It may occur due to abnormalities in glucoreceptors of β-cells, reduced sensitivity of peripheral tissues to insulin, reduction in number of insulin receptors and down regulation of these receptors[3].

GLOBAL STATUS OF DIABETES MELLITUS

There are an estimated 285 million adults with diabetes in 2010; this number will continue to increase globally due to an aging population, growth of population size, urbanization and high prevalence of obesity and sedentary lifestyle. Diabetes leads to both premature death and complications such as blindness, amputations, renal disease, and cardiovascular diseases[1]. India is a vast, heterogeneous country with an approximate population of 1.1 billion people, a complex socio-political history, and immense diversity of culture, dialects and customs. World Health Organization (WHO) reported 32 million people with diabetes residing in India, while the International Diabetes Federation (IDF) has reported an estimated 40.9 million for the same country. In either case, India remains the country with the highest absolute number of people with diabetes worldwide[4].

American Diabetes Association (ADA) Standards of Medical Care in Diabetes recommend a comprehensive disease management program that includes lifestyle interventions and use of oral antidiabetic agents (OADs) for the treatment of Type 2 Diabetes mellitus. Diabetic patients may experience the additive and/or adverse effects or tolerability issues associated with various OADs. For instance, sulfonylureas have been associated with weight gain and hypoglycemia, and patients on biguanides report negative gastrointestinal effects, while higher rates of weight gain, edema and fractures have been reported with thiazolidinediones[5]. Sometimes, patients may eventually require parenteral therapy with insulin or a glucagon-like peptide-1 (GLP-1) agonist[6]. As the presently available disease management strategies possess many patient incompatibilities, there is a need to discover more effective and safer antidiabetic agents by utilizing the rich heritage of medicinal plants.

MEDICINAL PLANTS OF RAJASTHAN WITH ANTIDIABETIC POTENTIAL

Rajasthan, the second largest state of the India exhibits variety in physiognomy, climate, soil and consequently the vegetation including a wide variety of medicinal plants[7]. The tribals of remote areas of Rajasthan are totally dependent on indigenous system of medicine for their healthcare as it is difficult for them to get modern medical facilities for their day-to-day health problems. The traditional healers of Rajasthan are having a commendable knowledge of the medicinal virtues of plants that grow around them[8]. Various ethnobotanical studies carried out in Rajasthan indicate that some plants (Table 1) are being used for their antidiabetic potential by most of the tribals; also prescribed by local vaids and bhopas (village priest).

***Acacia nilotica* (L.) Del. (Mimosaceae)**

Local Names: Babul, Bambul

It is a tree that can grow up to the height of 10 m. The gum obtained from the stem is locally used in confectionery and sweets. Bhils take this gum orally to cure diabetes[9].

Pharmacological Finding

1. A study was carried out to investigate the effect of an aqueous methanolic extract of pods on various biochemical parameters in alloxan-induced diabetic rabbits. Dose of 400 mg/kg body weight maximally reduced the blood glucose levels as compared to the diabetic group ($p<0.001$). This dose also significantly ($p<0.05$) lowered the plasma total cholesterol, triglyceride and low-density lipids (LDLs) in treated rabbits as compared to diabetic rabbits. This study revealed the antidiabetic potential of this plant[10].

***Acacia senegal* (L.) Willd. (Mimosaceae)**

Local Names: Kumat, Kumatio, Kumta

It is a small deciduous tree having smooth bark, pale-greenish grey in colour that peels off in flakes in older twigs[11]. It is found on the hillsides and gravel throughout the state[12]. The tree is extremely hardy and resistant to draught and is one of the main cash crops of the desert region[13].

This tree yields the true gum arabic which is used as binding agent in the manufacture of cough pastilles in pharmaceutical industries and for its demulcent and emollient action[14]. The Bhopas in Udaipur region prescribe the gum as a part of food for diabetic patients[9]. However, the antidiabetic potential of this plant has not been evaluated scientifically.

***Aegle marmelos* (L.) Corr. (Rutaceae)**

Local Names: Bel, Bel-patra

It is a small or medium sized tree that is sparsely scattered in mixed deciduous forests on the Aravalli range in Rajasthan and also often planted all over India and frequently near the Hindu temples[9, 15, 16]. The Garasia tribal take powder orally with water that is made up of roots, stem-bark and leaves to cure diabetes[9].

Pharmacological Findings

1. A study was carried out to evaluate the antidiabetic as well as the antioxidant potential of methanolic extract of leaves. In this study, alloxan induced diabetic rats were fed with the extract (suspended in distilled water) daily at the dose of 100 mg/kg body weight. Oxidative stress produced by alloxan was found to be significantly lowered by the administration of this extract. Results indicated that methanolic extract of leaves effectively reduced the blood sugar level as well as oxidative stress in experimental animals[17].

2. In another study, methanolic extract of the roots was fractionated into eight fractions using column chromatography. Antidiabetic activity of all the fractions was studied using the glucose uptake by isolated rat hemi-diaphragm *in vitro* model. The fractions coded as FB and FC enhanced the uptake of glucose by isolated rat hemi-diaphragm significantly ($p<0.001$) and was found to be more effective than insulin.

Using the bioassay-guided fractionation, two compounds 1 and 2 (Figure 1) were isolated from fraction FC by column chromatography and identified as 6-methyl-4-chromanone and skimmianine respectively by NMR and mass spectral methods[18].

3. Aqueous extract of seeds was administered orally at different doses (100, 250 and 500 mg/kg) to normal as well as sub (fasting blood glucose (FBG) normal; glucose tolerance abnormal) and mild (FBG 120–250 mg/dl) streptozotocin induced diabetic rats. The dose of 250 mg/kg was found to be the most effective dose and it decreased the blood glucose level (BGL) by 35.1% in normal healthy rats after 6 h of administration. The same dose also showed a marked reduction in BGL by 41.2% in sub and by 33.2% in mild diabetic rats in glucose tolerance test (GTT) after 2 h of administration. These results clearly indicated that aqueous seed extract possess antidiabetic effect in diabetic rats[19].

***Calotropis procera* (Aiton) R. Br. (Asclepiadaceae)**

Local Names: Madar, Aak, Aakro

It grows in the form of erect shrub or small tree and commonly found in wastelands and abundant in the desert throughout the year[9]. The tribals of Udaipur drink its root extract to cure diabetes and fever[9].

Pharmacological Finding

Petroleun ether, methanolic and aqueous extracts of leaves and roots were investigated for its hypoglycemic effect in streptozotocin induced diabetic male wister albino rats. The different extracts were administered at

dose of 250 mg/kg, as single dose per day to the experimental animals for a period of 15 days. The blood glucose level serum and lipid profile was determined in the diabetic rats. This investigation established the pharmacological evidence for antidiabetic folklore claim[20].

***Capparis decidua* Linn. (Capparidaceae)**

Local Names: Ker, Kario

It is a much branched, xerophytic shrub that grows up to 15 feet height[21]. It is common throughout the state and generally found on the rocks, gravel and sandy plains. Sometimes, it occurs on sand-dunes forming the chief feature of the landscape[12]. Unripe fruits are not only pickled locally, but also commercially. The mature fruits are eaten by the tribals. According to ethnopharmacological relevance, the dried fruits of *Capparis decidua* are used as an ingredient in antidiabetic compositions[9].

Pharmacological Finding

In a study, alkaloid rich fraction (AR) was obtained from dried fruits and evaluated for antidiabetic potential in streptozotocin induced diabetic mice at a dose of 50 mg/kg body weight for 28 days. On completion of the treatment, it significantly inhibited the acute elevation of blood glucose level and also reduced total cholesterol (TC) and triglyceride (TG) content ($p<0.05$). Activity of glucose-6-phosphatase (G6Pase) was attenuated by 44% and liver and muscle glycogen content showed significant improvement ($p < 0.05$). The expression of different target genes like G6Pase, phosphoenolpyruvate carboxykinase (PEPCK), aldose reductase and tumor necrosis factor-α (TNF-α) showed significant reduction whereas glucose transporter-4 (Glut-4), peroxisome proliferators activated receptor-γ (PPAR-γ) and glucokinase (GK) improved remarkably. This study clearly established the candidacy of AR fraction for further purification and characterization of the individual alkaloids, in order to understand their mechanism of action[22].

***Cassia auriculata* L. (Caesalpiniaceae)**

Local Names: Anwal, Tarwan, Tarawar

It is a tall, much branched shrub that grows up to 2 m height having reddish-brown smooth bark. It is found in gravelly and sandy soil throughout the state. Its bark provides one of the most important tanning materials[12]. Bhils take orally the fresh flowers with sugar to cure diabetes[9, 23]. Its seeds and leaves are also used in diabetes[9].

Pharmacological Findings

1. Leaf extract of this plant was studied for hypoglycemic activity in alloxan induced fasted diabetic rats and effect of this extract was also studied for glucose utilization by isolated rat hemi diaphragm method. For this purpose, ethanolic and water extract at a dose of 200 mg/kg per day was administered to diabetic rats for 10 consecutive days. A significant reduction in serum glucose level was observed from 3rd day to till the end of the experiment. During another study, the albino rats were killed by decapitation and diaphragms were exposed to Group I; tyrode solution with glucose (2000 mg/l) only, served as control, Group II; tyrode solution with glucose (2000 mg/l) + Insulin (0.25 IU/ml), Group III; tyrode solution with glucose (2000 mg/l) + extract of C. auriculata (25 mg/ml) and group IV; tyrode solution with glucose (2000 mg/l) + Insulin (0.25 IU/ml) + extract of *C. auriculata* (25 mg/ml). Glucose uptake and glycogen deposition studies suggested that leaf extract probably has no direct insulin like effect which can enhance the peripheral utilization of glucose[24].

2. Aqueous extract of leaves was evaluated for antihyperglycemic and hypolipidemic activity in streptozotocin induced mild diabetic (MD) and severe diabetic (SD) rats. The extract was orally administered to MD and SD rats at 100, 200 and 400 mg/kg doses for 1 day to determine antihyperglycemic activity. The 400 mg/kg dose was administered daily for 3 weeks to assess glycemic control and hypolipidemic effect. A dose dependant fall in fasting blood glucose was observed after 5 h of extract administration in diabetic rats. After 3 weeks treatment, extract produced significant reduction in fasting blood glucose and glycosylated haemoglobin in both MD and SD rats. Serum lipid levels were reversed towards normal in extract fed MD and SD rats. It demonstrated that this plant possesses potent antihyperglycemic and hypolipidemic activity in both MD and SD rats[25].

***Cassia sophera* L. (Caesalpiniaceae)**

Local Name: Kasunda

It is a shrub that is found chiefly in the east of Aravalli and rarely found in wastelands. Bhils of eastern Rajasthan mix its bark and seed powder in honey and give to the diabetic patients to eat[9, 26].

Pharmacological Finding

Aqueous and methanol extracts of seeds has been reported to possess significant hypoglycemic activity in alloxan induced diabetic rabbits[27].

***Cayratia trifolia* (L.) Domin (Vitaceae)**

Local Names: Char, Char-bel, Khhata nimba

It is a climbing or spreading herb or undershrub with 3-foliate leaves[9,28,29]. It is easily found in Sitamata wildlife sanctuary of Chittorgarh and Udaipur district located in south-west region of the state[28]. It stem, leaves and root contain hydrocyanic acid and leaves also contain delphinidin, cyanidin and yield yellow waxy oil and

sterols[13]. Bhils of Udaipur region take orally the extract of roots to cure diabetes[9]. The extract of tuber of this plant along with the infusion of its seeds is given orally to diabetic patients to check the sugar level of blood[29]. However, the antidiabetic potential of *Cayratia trifolia* has not been evaluated scientifically.

***Cyamopsis tetragonoloba* (L.) Taub. (Fabaceae)**

Local Names: Guar, Ganwar, Gwar

It is an annual herb that is cultivated as a rainy season crop for edible fruits, seeds and fodder throughout the state[9,15]. The young pods are consumed as vegetable and whole plant is used as a green manure[12]. Tribals of the desert soak the seeds in water in the evening and drink that water in the next morning to cure diabetes[9].

Pharmacological Finding

Aqueous extract of beans was investigated for fasting blood glucose levels in glucose loaded normal and alloxan induced diabetic rats. Aqueous extract of beans at 250 mg/kg body weight significantly lowered blood glucose levels in diabetic rats within 3 hr of administration. Continued administration of the extract at the same dose daily for 10 days produced statistically significant reduction in the blood glucose levels indicating the hypoglycemic potential of beans of this plant[30].

***Dalbergia sisso* Roxb. (Fabaceae)**

Local Name: Sisham

It is a deciduous tree that is common in wastelands, along the roads and boundaries of gardens[9]. It yields a valuable timber that has high industrial and commercial value[9,12]. Tribals of Dungarpur district take orally the paste of leaves to cure diabetes[9].

Pharmacological Finding

In a study, the ethanolic extract of leaves was administered orally at the doses of 250 and 500 mg/kg to normal rats. Dose of 500 mg/kg was found to be more effective; it decreased blood glucose level (BGL) by 38.2 % in normal healthy rats after 1 day of administration. After daily treatment with both the doses of extract for 21 days to alloxan induced diabetic (FBG 300-350 mg/dL) rats, the BGL reduced to 125 mg/dL by 250 mg/kg and 104 mg/dL by 500 mg/kg. This study indicated the hypoglycemic and antihyperglycemic potential of the extract[31].

***Gymnema sylvestre* (Retz.) R. Br. (Asclepidaceae)**

Local Names: Jangli-urad, Gurmar

It is a much branched, twining woody climber running over the tops of small trees[32]. It is frequently found in the deciduous forests in the east of Aravalli[9]. Its leaf extract contain gymnemic acid which is said to inhibit hyperglycemia. It abolishes the taste of sugar and is believed to neutralize the excessive sugar present in the body of diabetic patient[32]. It is used as a remedy for diabetes throughout the state[9].

Pharmacological Findings

1. In a study, aqueous extract of leaves was administered orally at the dose of 400, 600 and 800 mg/kg for 30 days. Fasting blood glucose, cholesterol, HDL cholesterol and serum triglyceride levels were estimated in both normal and alloxan induced diabetic rats. All these levels were found to be significantly reduced in treated rats. It revealed that this plant possess significant antidiabetic and hypolipidemic activity and seems promising for the development of a phytomedicine for treatment of diabetes mellitus[33].

2. In another study, an active compound-dihydroxy gymnemic triacetate (Figure 2) has been isolated from its acetone extract. This compound at a dose of 20 mg/kg body weight was administered orally for 45 days to streptozotocin diabetic rats for the assessment of various biochemical parameters in normal and diabetic rats. This compound produced significant effects on all biochemical parameters in comparison to diabetic control group. Results indicated the hypoglycemic and hypolipidemic activity of dihydroxy gymnemic triacetate on long-term treatment and it could be used as a drug for treating diabetes[34].

***Momordica charantia* L. (Cucurbitaceae)**

Local Names*:* Karela, karelo

It is a monoecious climber and cultivated for its fruits cooked as vegetable. Local vaids prescribe its vegetable to the diabetic patients[9]. It is a medicinal plant and used in Ayurveda for treating various diseases including diabetes mellitus[35].

Pharmacological Findings

1. Aqueous extract of fresh unripe whole fruits at a dose of 20 mg/kg body weight was found to reduce fasting blood glucose by 48%, comparable to the standard drug-glibenclamide. This extract was tested for nephrotoxicity, hepatotoxicity and biochemical parameters such as SGOT, SGPT and lipid profile. The extract did not show any signs of nephrotoxicity and hepatotoxicity as judged by histological and biochemical parameters. Thus the aqueous extract was proved as a safe alternative for reducing blood glucose level[36].

2. In vitro and in vivo experiments were carried out to study the role of juice of fruits on the diabetic status. Control and streptozotocin induced diabetic mice were fed orally daily once with either 10, 50 or 100% juice (0.2 ml juice equivalent to 10 ml/kg body weight) for a period of 5 days. Activity of the juice was tested on streptozotocin treated RIN cells (rat insulinoma cell line) and isolated islets in vitro. Feeding with juice caused reduction in streptozotocin-induced hyperglycemia in

mice. Further it also reduced the streptozotocin-induced apoptosis in RIN cells indicating the mode of protection of RIN cells, islets and pancreatic β-cells[35].

3. Acetone extract of whole fruit was studied at the doses of 25, 50 and 75 mg/100 g body weight in alloxan induced diabetic rats. Histological observations showed the different phases of recovery of β-cells of the islets of Langerhans of pancreas, which were less in number in the untreated diabetic rats proving the antidiabetic potential of this plant[37].

***Syzygium cumini* (L.) (Myrtaceae)**

Local Names: Jamun, Jambus

It is an evergreen tree having grayish brown branches[21]. Local vaids prescribe the mature fruits to the diabetic patients[9]. Leaves, seeds, wood and stem bark are also used in treatment of diabetes[32]. An aqueous extract of seeds found to cause the marked, prolonged decrease in blood sugar upon hypodermic injection into dogs[16].

Pharmacological Finding

Oral administration of petroleum ether, chloroform, acetone, methanolic, and water extracts at a dose of 100 mg/kg, p.o. for 21 days caused a decrease in fasting blood sugar (FBS) in diabetic rats. Among all the extracts, methanolic extract was found to lower the FBS significantly in diabetic rats. This extract was subjected to column chromatography that led to the isolation of an active principle, Cuminoside (a phenolic glycoside). It was studied for its hypoglycemic and antioxidant potential at the dose of 50 mg/kg, p.o. and a significant decrease in FBS level, lipid peroxidation level, and improvement in the levels of antioxidant enzymes was observed in diabetic rats. This study provided a scientific rationale for the use of cuminoside as an antidiabetic agent[38].

***Withania somnifera* (L.) (Solanaceae)**

Local Names: Ashgandh, Chirpotan, Rashbhari

It is a much branched, erect, perennial undershrub that grows up to the height of 1.5 m[20]. It is common in moist and shady habitats[9,12]. It is an Ayurvedic medicinal plant that is popular home remedy for several human ailments. It is mentioned in Vedas as an herbal tonic and health food. Infusion of leaves is prescribed by local vaids as a medicine to cure diabetes[9]. Its roots also exhibit hypoglycemic activity[32].

Pharmacological Findings

1. Hypoglycaemic and hypolipidaemic effects of extracts of root and leaves were investigated at doses of 100 and 200 mg/kg body weight in alloxan induced diabetic rats. After 8 weeks of treatment with the extract, a significant decrease was observed in the levels of urine sugar, blood glucose, glycosylated haemoglobin, liver glucose-6-phosphatase, aspartate transaminase, alanine transaminase, acid phosphatase, alkaline phosphatase, serum lipids except high density lipoprotein-bound cholesterol. It indicated the hypoglycemic and hypolipidaemic activity of root and leaf extract of this plant[39].

2. Hypoglycemic, diuretic and hypocholesterolemic effects of roots were assessed on human subjects. 6 mild NIDDM subjects and 6 mild hypercholesterolemic subjects were treated with the powder of roots for 30 days. Various parameters were studied in the blood and urine samples of the subjects along with dietary pattern before and at the end of treatment period. Decrease in blood glucose was comparable to that of standard drug. Significant increase in urine sodium, urine volume, significant decrease in serum cholesterol, triglycerides, LDL and VLDL were observed and indicated the hypoglycemic, diuretic and hypocholesterolemic activities of root[40].

CONCLUSION

Research studies have a role in highlighting inequalities and improving comprehension of the complex mix of predisposing and modifiable factors associated with a particular disease. The research in alternative system of medicine indicates that further exploration of natural resources is required to establish the pharmacological activities and to find the active constituents for the development of drugs. These studies provide the right blend of evidence to stimulate the modification of current medical practices. Geno- and phenotypically, the Asian Indian population are at elevated risk for developing diabetes in comparison to other population groups. Therefore, the well planned, dedicated, and diligent care should be a priority for diabetes patients. Plant origin based drugs have been utilizing from many years in patients with insulin dependent and non-insulin dependent diabetes. Scientific evaluations of the plant species have proved their efficacy for serving as the hypoglycemic agent. Conclusively, the integration of research in alternative system of medicine and clinical practice is must in seeking sustainable, practical, scientific, and socially acceptable models for diabetes care.

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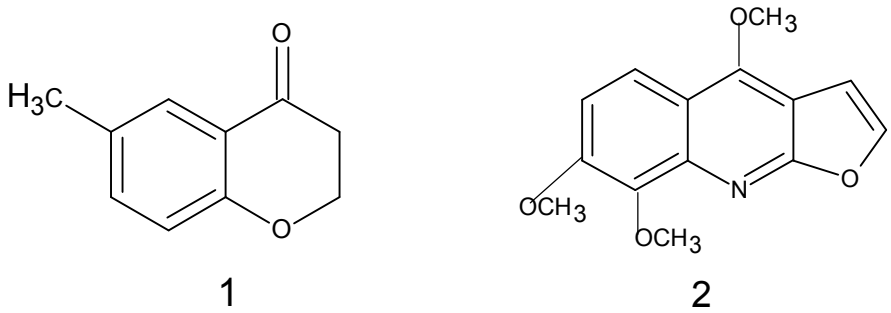
TABLE 1: IT SHOWS MEDICINAL PLANTS OF RAJASTHAN WITH ANTIDIABETIC POTENTIAL

S. No.	Name of plant, Family	Part used	Extract/Active constituent
1.	*Acacia nilotica* L. Del., Mimosaceae	Gum, stem bark, pods	Aqueous-methanol extract
2.	*Acacia senegal* L. Willd., Mimosaceae	Gum	--
3.	*Aegle marmelos* L. Corr., Rutaceae	Fruits, stem bark, root, leaves	Aqueous & methanol extracts/ 6-methyl-4-chromanone, skimmianine
4.	*Calotropis procera* (Aiton) R. Br., Asclepiadaceae	Root, leaves	Petroleum ether, aqueous & methanol extracts
5.	*Capparis decidua* Linn., Capparidaceae	Fruits, stem bark, flower	Alcoholic extract/ Alkaloid rich fraction
6.	*Cassia auriculata* L., Caesalpiniaceae	Leaves, seeds, flower	Aqueous extract
7.	*Cassia sophera* L., Caesalpiniaceae	Stem bark, seeds	Aqueous & methanol extracts
8.	*Cayratia trifolia* L. Domin, Vitaceae	Root, seeds	Infusion
9.	*Cyamopsis tetragonoloba* L. Taub., Fabaceae	Gum, pods	--
10.	*Dalbergia sisso Roxb.*,Fabaceae	Leaves	Ethanol extract
11.	*Gymnema sylvestre* (Retz.) R. Br., Asclepidaceae	Leaves	Aqueous extract/ Dihydroxy gymnemic triacetate
12.	*Momordica charantia* L., Cucurbitaceae	Fruits	Acetone, alcoholic & aqueous extracts
13.	*Syzygium cumini* L., Myrtaceae	Fruits, stem bark, seeds, leaves	Methanol extract/ Cuminoside (phenolic glycoside)
14.	*Withania somnifera* L., Solanaceae	Leaves, root	Alcoholic extract



1 2

Figure 1: It shows the structures of compound 1 (6-methyl-4-chromanone) and compound 2 (skimmianine)

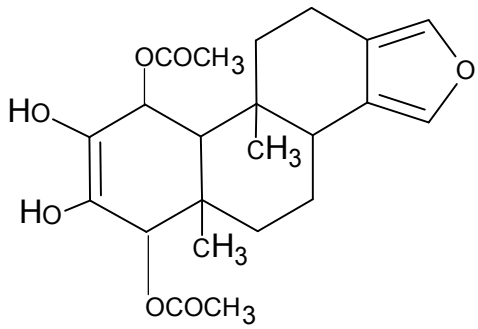


Figure 2: It shows the structure of dihydroxy gymnemic triacetate isolated from acetone extract of *Gymnema sylvestre*